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Effects of 30%, 50%, 70%VO2 max treadmill exercises on gut microbiome of atherosclerotic mice

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Objective To observe the dynamic changes of gut microbiome in mice before and after different intensities of treadmill exercises, and to explore the effects of different intensities of treadmill exercises on gut microbiome of atherosclerotic (AS) mice.

Methods The 50 male ApoE^{-/-} mice aged 8 weeks were randomly divided into 2 groups, 10 mice in the general feeding group and the other 40 mice in the AS group, which were fed with normal and high-fat diet for 4 weeks respectively. Weight and blood test were taken before and after 4 weeks feeding. The serum Triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein (HDL) levels were examined by blood test in ApoE^{-/-} mice model, and atherosclerotic disease degeneration score of adult mice was used to determine the success of modeling after 4 weeks feeding. Then two mice selected from the normal and high-fat group respectively selected to test the maximum oxygen uptake (VO2 max) by the reformative Bedford method, and the running platform speed and slope corresponding to 30%, 50% and 70%VO2 max were determined. The 40 AS mice were randomly divided into the model blank group, the lowintensity exercise group, the medium-intensity exercise group and the high-intensity exercise group according to their weight for 4 weeks of exercises, respectively. The low-intensity exercise group was 30% VO2 max, with a slope of 10 degrees and a speed of 10 m/min. The medium intensity exercise group was 50% VO2 max with a slope of 10 degrees and a speed of 15 m/min. The high-intensity exercise group was 70% VO2 max with a slope of 10 degrees and a speed of 20 m/min. The exercises were performed for 4 weeks, 5 days a week, 20 minutes a day. The fresh feces were collected from 5 groups of mice before and after 4 weeks treadmill exercises. The number of gut Lactobacillus, Bacteroides, Firmicutes, Bifidobacterium, Verrucomicrobiaceae, Akkermansia, Escherichia coli, *Collinsella and Clostridium* in AS mice were analyzed by 16s sequencing.

Results 1. The TG, TC and LDL-C were significantly increased in the blood serum of the mice after the modeling, and the HDL-C was decreased, and the atherosclerotic disease degeneration score was significantly increased in the adult mice, and the modeling was successful. 2. The different intensity treadmill exercises can increase the number of gut probiotics in mice and decrease the number of harmful bacteria. The beneficial bacteria in gut tract of AS mice with moderate intensity of 50% VO2max was observed in the experiment: *Bacteroides, Bifidobacterium and*

Verrucomicrobiaceae, Akkermansia were significantly increased, P<0.05. The harmful bacteria:Lactobacillus, Escherichia coli, Collinsella and Clostridium were significantly decreased, P<0.05. The ratio of *Firmicutes / Bacteroidetes* was increased.

Conclusions 1. High-fat diet can lead to AS in ApoE^{-/-} mice. 2. The different intensity treadmill exercises can reduce the weight of AS mice. 3. The number and abundance of probiotics of gut microbiome of AS mice could be promoted by different intensity treadmill exercises, among which the medium intensity aerobic exercise can significantly increase the number of beneficial bacteria such *Bacteroidetes, Bifidobacteria, Verrucomicrobiaceae* and *Akkermansia*, meanwhile, the structure of gut microbiome in AS mice was improved as well.